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MCO® Dialyzers: Enhanced Selectivity High-Flux

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Background and Introduction

End stage renal disease patients on hemodialysis have an increased mortality risk compared to the general population, which indicates that research on renal replacement therapy is required to improve patients' outcomes.

In this respect, one of the unmet needs in hemodialysis is the adequate removal of uremic toxins in a broad molecular weight range. Therefore, patients on hemodialysis present higher levels of middle and large molecular solutes in plasma.

MCO®, a newly designed high flux (HF) dialyzer based on medium cut-off technology, should provide improved selectivity to extend the spectrum of middle and large toxins removed during treatment.

Here we assess the in vitro performance of the MCO® devices in simulated hemodialysis (HD) and hemodiafiltration (HDF) treatments.

Methods

Middle and large molecule clearances of four different MCO® prototypes (Gambro), Elisio 17H (Nipro), FX CorDiax80, and FX CorDiax800 (Fresenius) dialyzers were compared.

HD and HDF treatments were simulated with 300 ml/min or 400 ml/min blood flow and 700 ml/min dialysate flow; high volume HDF was simulated with additional ultrafiltration rate of 100 ml/min (corresponding to convection volume of 24 L in a 4h treatment).

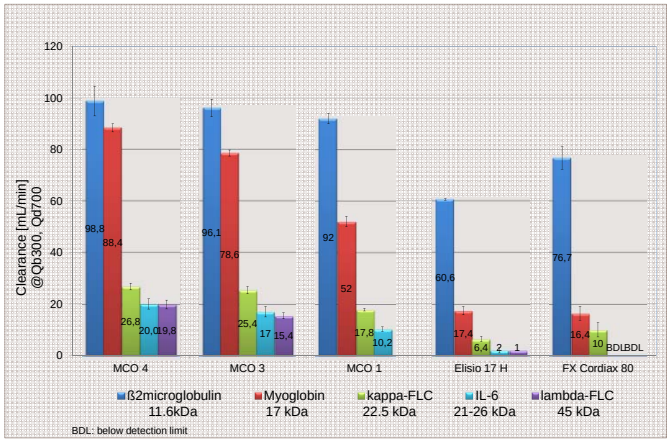
In each experiment (n=3), 1 L of uniform human plasma (octaplas®LG, protein concentration 60 g/L) was recirculated for 60 min and followed by a 60 min simulated treatment. Markers were spiked into the plasma pool after 55 min of recirculation: human beta2-microglobulin (5 mg), human myoglobin (500 µg), kappa-FLC (~300 mg), and lambda-FLC (150 mg), while interleukin 6 was comprised in the human plasma.

Samples were taken from the pool after defined time intervals. The concentration of markers in the pool and samples was measured by nephelometry and the clearance was calculated from the first order kinetics for the variation of the pool concentration in time.

Results

The four MCO® prototypes differ in permeability, which can be evidenced in the in vitro clearances measured during the simulated treatments.

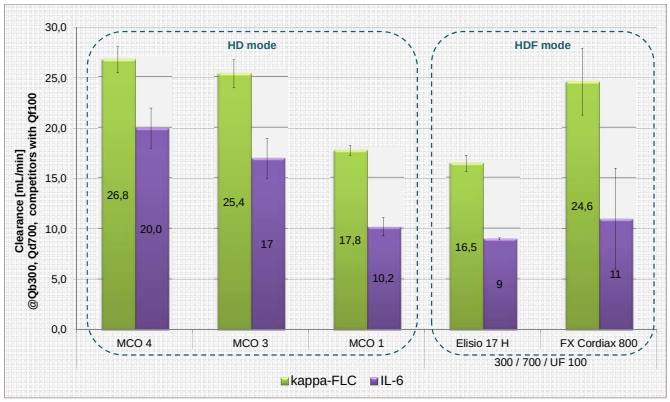
Figure 1: In vitro clearance comparison for middle and large molecules during simulated HD treatment with Q_B = 300 ml/min



In vitro clearances for the MCO® devices during the simulated HD treatments were consistently higher than those shown by Elisio and CorDiax.

For the largest markers, i.e., IL-6 (21 kDa) and λ-FLC (46 kDa), Elisio showed decline in the concentration in the pool, while the clearance values for CorDiax were not possible to calculate through kinetic fitting (below detection limit = BDL).

Figure 2: In vitro clearance of MCO prototypes for large solutes in simulated HD compared to simulated HDF with Q_B = 300 ml/min



The clearances for simulated HDF treatments show the effect of high volume convective therapy in increasing large molecules removal.

Fig. 2 compares the clearances for molecules above 20 kDa. The improved selectivity of the MCO® devices enables higher clearances in HD mode, which are similar or even higher than those measured under high volume HDF condition.

Table 1: In vitro clearances in simulated HD and high volume HDF treatment with Q_B = 400 ml/min

Devices	Treatment	Clearances (Q_B = 400ml/min)			
		b2m	Myo	k-FLC	IL-6
MCO® 3	Hemodialysis	106 ± 4	83 ± 1	27 ± 2	18 ± 1
MCO® 2	Hemodialysis	102 ± 3	65 ± 1	23 ± 1	16 ± 3
MCO® 1	Hemodialysis	93 ± 5	61 ± 1	20 ± 1	12 ± 2
FX CorDiax 80	Hemodialysis	85 ± 10	19 ± 2	11 ± 1	BDL
FX CorDiax 800	High volume HDF	126 ± 7	33 ± 2	24 ± 1	9 ± 2

BDL: below detection limit

Results of simulated treatments run with blood flow of 400 ml/min show similar tendencies as with 300 ml/min. The MCO® prototypes show higher clearances when compared in HD mode.

When the performance is compared to high volume HDF, MCO® devices show higher clearances for myoglobin and IL-6, higher or similar clearances for κ-FLC and lower clearances for β2-microglobulin.

Conclusions

MCO® dialyzers tested in regular HD mode deliver in-vitro clearances:

- Superior to conventional high-flux membranes in HD mode
- Equivalent to slightly superior removal of myoglobin, κ-FLC and IL6 compared to Elisio and CorDiax in High Volume HDF (convection volumes=24 L)

Clinical studies are ongoing in order to confirm the in-vitro findings.

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